REMARKS

The following remarks address the substance of the Office Action.

I. **Rejection of Claims 1-23 and 38-39 Under 35 U.S.C. §112, Second Paragraph**

The Examiner has rejected Claims 1-23 and 38-39 under 35 U.S.C. §112, second paragraph on the assertion that the recitations of the terms: "detecting", "original", "a unique set of primers", "at least part of original nucleotide sequences into target", "preferably", "specific of an organism", "forms results in said signal at the expected locations" in Claims 1-23 and 38-39; as well as "the amplified homologous original sequence" in claims 2 and 4; "the same primer pair" in claims 3-5; "mRNA first retrotranscribed into cDNA" in claim 4; "the copy of the homologous original nucleotide sequences" in Claim 5; "the same capture nucleotide sequences specific for one organism" in Claim 6; "the specific sequence of the capture sequence" in claims 7-8; "superior to 10 fmoles" in Claim 9; "presents an homology" in Claim 10; "such as" in Claim 12; "mixture thereof" in Claim 13; "submitted to a retro-transcription", "at 3' or 5' end", "possibly", and "stopper sequence" in Claim 14; "capture nucleotide sequences specific of the homologous sequences specific for the binding with the homologous target nucleotide sequence together with a consensus sequence or a common detection" in claim 16; as well as improper Markush groups in claim 15; "the original sequence" in claims 18-23 are vague and indefinite. The Applicants have amended 1, 2, 4, 8-10, 12-16, 18-23 and canceled claims 3, 5, 6, 7, 11, and 39. The amended claims now do not recite the above-listed terms.

The Examiner also asserted that the Specification does not describe or define the MAGE, HLA-A, protein G, and cytochrome p450 families. The Applicants respectfully disagree. MAGE are known in the art as Melanoma antigens that are thought to induce a tumor-specific immune response and to be potential therapeutical targets for cancer immunotherapy. The Specification lists 12 MAGE family members (see paragraph **[0105]** of the Substitute Specification). HLA is known by a skilled artisan to be a human leukocyte antigen – a major histocompatibility complex class I molecule. The Specification lists 14 capture probes for 14 various HLA-A subtypes (see paragraph **[0122]** of the Substitute Specification). Protein G (or G-protein) family is also well-defined and well-known family of proteins and is a common knowledge among skilled artisans. The Specification lists 5 G-protein-coupled Dopamine receptors (paragraph **[0111]**), 3 G-protein-coupled Histamine receptors (paragraph **[0115]**), and

14 G-protein-coupled Serotonin receptors (paragraph **[0118]**). Cytochrome p450 is also well-known in the art to be an electron-carrying enzyme that inserts one of the oxygen atoms of the molecule O_2 into its substrates. It is found in animals, plants, and bacteria. It plays an important role in mammalian livers and the making of steroid hormones in the adrenal cortex. Cytochrome P450 enzymes are known to metabolize the majority of drugs, to detoxify environmental pollutants as well as to activate some classes of carcinogens as polycyclic aromatic hydrocarbons or nitrosamines. The Specification lists five p450 subtypes (see paragraph **[0126]**). Therefore, the Applicants assert that Claims 18-23 are definite in recitation of MAGE, HLA-A, protein G and p450 families.

Accordingly, Applicants respectfully request withdrawal of the rejection of Claims 1, 2, 4, 8-10, 12-16, and 18-23 under 35 U.S.C. §112, second paragraph.

II. Rejection of Claims 1-14, 18-23 and 38-39 under 35 U.S.C. §102(b)

The Examiner has rejected Claims 1-14, 18-23 and 38-39 under 35 U.S.C. §102(b) over Brown *et al.* (USPN 5,807,522). Applicant respectfully maintains that Brown *et al.* does not anticipate the subject matter encompassed by Claims 1-14, 18-23 and 38-39. To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ...There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). Brown *et al.* discloses a microarray of polynucleotide biopolymers that are non-covalently bound to the surface of the substrate and that hybridize to cDNAs obtained from various samples. Brown *et al.* does not disclose or even suggest single-stranded capture nucleotide sequences bound in an array to an insoluble solid support via a spacer which is at least 6.8 nm in length. Furthermore, Brown does not teach nor suggest amplifying at least two of homologous nucleotide sequences in a sample using the same primer pair, nor does Brown et al. teach discrimination of homologous sequences on an array. Thus, because Brown *et al.* fails to teach or suggest a single-stranded capture nucleotide sequences bound in an array to an insoluble solid

support via a spacer which is at least 6.8 nm in length to identify homologous nucleotide sequences that are amplified using the same primer pair, Applicants respectfully assert that Brown does not anticipate any of amended Claims 1, 2, 4, 8-10, 12-16, 18-23, and 38, or new claims 40-45. Accordingly, Applicants request withdrawal of the §102(b) rejections.

The Examiner has rejected Claims 1-14, 18-23 and 38-39 under 35 U.S.C. §102(b) over Fodor *et al.* (USPN 5,800,992). Applicant respectfully maintains that Fodor *et al.* does not anticipate the subject matter encompassed by Claims 1-14, 18-23 and 38-39. Fodor *et al.* discloses a substrate with a surface having a microarray of at lest 10^3 distinct polynucleotide or polypeptide biopolymers in a surface area of less than 1 cm^2. Each distinct biopolymer is bound non-covalently to a coating of the surface and is capable of hybridizing to various cDNAs. Fodor *et al.* does not disclose or even suggest single-stranded capture nucleotide sequences bound in an array to an insoluble solid support via a spacer which is at least 6.8 nm in length. Furthermore, Fodor does not teach nor suggest amplifying at least two of homologous nucleotide sequences in a sample using the same primer pair.

In addition, as discussed below with respect to new Claim 45, Fodor et al. fragment the target nucleotide sequences to be detected and detect a pattern of spots resulting from the binding of such fragments to several small capture probes.

For the foregoing reasons, Applicants respectfully assert that Fodor does not anticipate any of amended Claims 1, 2, 4, 8-10, 12-16, 18-23, and 38, or new claims 40-45. Accordingly, Applicants request withdrawal of the §102(b) rejections.

III. Rejection of Claims 15-17 under 35 U.S.C. §103(a)

The Examiner has rejected Claims 15-17 under 35 U.S.C. §103(a) over Brown *et al.* or Fodor *et al.* (USPN 5,800,992), and further in view of Vannuffel *et al.* (WO 99/16780) on the assertion that it would have been obvious at the time the invention was made to modify the method of Brown or Fodor by including the primers and probes specific for the *femA* sequence of Staphylococci to detect specific species of the Staphylococci genus in diagnosing infections. The Applicant respectfully disagrees.

As discussed above, neither Brown nor Fodor disclose arrays in which capture nucleotide sequences are bound to an insoluble support by a spacer which is at least 6.8 nm in length. This feature of the claimed invention is also not disclosed in Vanuffel.

Vannuffel describes reverse hybridization assay of PCR amplified *FemA* gene fragments using *Staphylococcus*-specific probes immobilized on nylon membranes. The FemA amplicons were hybridised to the immobilised probes and then revealed using a streptavidin-peroxidase conjugate and the DAB substrate. There is no suggestion in Vannuffel to attach the probes to the solid support via a spacer which is at least 6.8 nm in length. As discussed above, Brown and Fodor also do not suggest such a spacer.

Because none of the cited references teach or suggest arrays in which capture nucleotide sequences are bound to an insoluble support by a spacer which is at least 6.8 nm in length, the cited references do not render Claims 15-17 obvious under 35 U.S.C. §103(a). The Applicants respectfully request withdrawal of the rejection of Claims 15-17 over Brown *et al.* or Fodor *et al.* (USPN 5,800,992), and further in view of Vannuffel *et al.* (WO 99/16780).

CONCLUSION

The Substitute Specification is submitted herewith as requested by the Examiner. The current amendments to the Substitute Specification address the typographical, spelling and grammatical errors and do not introduce new matter. Support for the amendment to paragraph **[0088]** can be found in the Figure 3 as filed.

Claims 3, 5, 6, 7, 11, and 39 have been canceled without prejudice, and Claims 1, 2, 4, 8-10, 12-16, 18-23, and 38 have been amended to more precisely claim the invention according to conventional practice before the US PTO. New Claims 40-45 have been added. Thus, claims 1, 2, 4, 8-10, 12-23, 38, and 40-45 are presented for examination. Support for the amendments to Claim 1 can be found in the original claims 7 and 24. Support for the new Claim 40 can be found in Claim 9 as filed; support for the new Claims 41 and 42 can be found in Claim 10 as filed; support for the new claim 43 can be found in the Substitute Specification in paragraphs **[0035]-[0036]**. Support for the new Claim 44 can be found in the original Claim 12.

Support for the new Claim 45 can be found in the Substitute Specification, for example, on page 5, paragraph **[0019]**. No new matter has been introduced herein. With respect to new

Claim 45, Applicants note that, as provided in the Substitute Specification on page 5, paragraph **[0019],** the detection of a single spot signal at one specific location on said insoluble solid support is a significant advantage over prior art methods, including the method described in the Fodor reference, which involve detection using a pattern of spots. Applicants note that by "detection of a single spot signal at one specific location" Applicants refer to detection using a single capture nucleotide sequence for specific binding of a target sequence and that binding of the target sequence to the capture molecule generates a spot. However, "detection of a single spot signal at one specific location" does not require that only a single spot on the array is used to detect the target since more than one capture sequence can be present and binding of a target sequence to these capture molecules will generate more than one spot.

In view of the foregoing, Applicants respectfully submit the present application is fully in condition for allowance. If any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number listed below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: April 23, 2003

By: _____

Daniel Hart
Registration No. 40,637
Attorney of Record
Customer No. 20,995
(619) 235-8550

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